Poly(methacrylic acid)-based single-chain polymer nanoparticles for targeting and imaging pancreatic tumors *in vivo*

Marco Marradi[1], Ana B. Benito[1], Miren K. Aiertza[1], Larraitz Gil-Iceta[2], María Jiménez-González[2], Boguslaw Szczupak[2], Torsten Reese[2], Eugenio Scanziani[3,4], Lorena Passoni[3], Michela Matteoli,[3] Marcella De Maglie,[3,4] Arie Orenstein[5], Mor Oron-Herman[5], Gennady Kostenich[5], Ludmila Buzhansky[6], Talia Shekther Zahavi[6], Ehud Gazit[6], Hans-Jurgen Grande[1], Vanessa Gomez-Vallejo[2], Jordi Llop[2] and Iraida Loinaz[1]

[1]IK4-CIDETEC, Biomaterials Unit, - , Spain; [2] - , Spain; [3]Fondazione Filarete, Viale Ortles 22/4, 20139 Milano, Italy; [4]Dipartimento di Medicina V , Via Celoria 10, 20133, Milan, Italy; [5]The Advanced Technologies Center, Sheba Medical Center, Tel Hashomer 52621, Israel; [6]Department of Molecular Microbiology and Biotechnology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Ramat Aviv, Tel Aviv 69978, Israel
mmarradi@cidetec.es

Cancer accounted for 8.2 million deaths worldwide in 2012 and, for some types of cancer, e.g. pancreatic adenocarcinoma incidence equals mortality [1]. The development of tools for the early diagnosis of pancreatic adenocarcinoma is an urgent need in order to increase treatment success rate and reduce patient mortality.

Here, we present a modular nanosystem platform integrating soft nanoparticles with a targeting peptide and an active imaging agent for diagnostics. Biocompatible single-chain polymer nanoparticles (SCPNs) based on poly(methacrylic acid) were prepared and functionalized with the somatostatin analogue PTR86 as the targeting moiety (Figure 1), since somatostatin receptors are overexpressed in pancreatic cancer.

The gamma emitter ^{67}Ga was incorporated by chelation and allowed *in vivo* investigation of the pharmacokinetic properties of the nanoparticles using single photon emission computerized tomography (SPECT). The resulting engineered nanosystem was tested in a xenograph mouse model of human pancreatic adenocarcinoma. Imaging studies demonstrated that accumulation of targeted SCPNs in the tumor is higher than that observed for non-targeted nanoparticles due to the improved retention of the nanocarrier in this tissue [2].

References

[1] Ferlay *et al*., Eur. J. Cancer, 49 (2013) 1374.
[2] Benito *et al*., Biomacromolecules, 17 (2016) 3213.

Figures

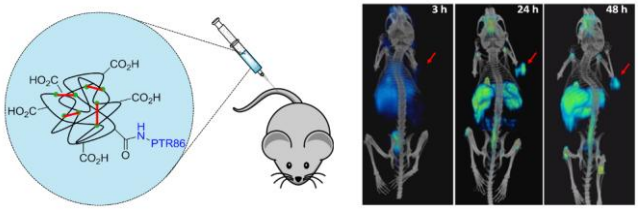

Figure 1: Water dispersible, radiolabeled and targeted single-chain poly(methacrylic acid) (PMAAc) nanoparticles were injected into mice bearing subcutaneous human pancreatic ductal adenocarcinoma. Imaging studies were performed *in vivo* by SPECT at different times.